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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DAVIS, MINH TAM B	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 02/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/840,746	CHEN ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 August 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *28 August 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attached*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *none*.

Claim(s) objected to: *none*.

Claim(s) rejected: *1-6*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☒ Other: *See Continuation Sheet*

Continuation of 3. Applicant's reply has overcome the following rejection(s): 112, first paragraph, scope, item 1, concerning "encoding" a polypeptide issue.

Continuation of 10. Other: Note the attached two new references, which are necessitated to response to Applicant arguments.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant cancels claims 13-20. Applicant retains claims 7-12, arguing that they are methods of use of the composition of claim 1 and 3, depend from and are the same scope as claims 1 and 3, and therefore subject to rejoinder pending allowance of claims 1 and 3 in accordance with *In re Ochiai* and MPEP 821.04.

Accordingly, claims 1-6 are being examined.

The submission of the Declaration by Dr. Tod Bedilion is acknowledged and entered.

The following are the remaining rejections.

REJECTION UNDER 35 USC 101, UTILITY

Applicant submits the Declaration by Dr. Tod Bedilion.

Applicant argues that Applicant has provided several published articles attesting the facts that the BT20 cell line is commonly used as a model system for determining gene expression pattern in breast cancer (see Lee et al, Mitchell, Williamson, and Chen). Applicant argues that the fact that the Witsuba article does not specificially recite this cell line does not provide evidence one way or the other as to its usefulness in modeling human breast cancer. The Witsuba article was recited in the specification as an example of the established usefulness of human mammary epithelial cells at various

stages of breast cancer in studying malignant transformation and tumor progression of the disease.

Applicant asserts that the data in Table 1 is not derived from electronic Northern analysis, but from a microarray format. Applicant challenges the Examiner's contention that the cDNA databases, such as LIFESEQ database recited in the instant specification are underepresentative of actual expressed gene, because Applicant has provided a published article reciting that the most recent estimates of the human genome projected approximately 30,000 genes, considerably less than the 100,000 figure provided by the Examiner.

The submission of the Declaration by Dr. Tod Bedilion is acknowledged and entered.

This argument is not found to be persuasive. Although the BT20 cell line is commonly used for determining gene expression pattern in breast cancer (see Lee et al, Mitchell, Williamson, and Chen), none of the references teach that the BT20 cell line is a model system for in vivo studying of breast cancer.

Further, although some of the breast cancer cell lines studied by Wistuba et al have correlation with their corresponding tumor tissue, concerning various criteria such as morphological features, presence of aneuploidy, immunohistochemical expression of estrogen receptors etc.., it seems that the cell lines studied by Wistuba et al are only from a specific subset of primary breast carcinoma. The breast cell line BT20 used in the claimed invention, however, seems not to be from the same subset of primary breast carcinoma taught by Wistuba et al. Further, the period of culture of the cell lines

studied by Wistuba et al during which the retention of the parental tumors are retained is only up to 60 months. It is not clear how long the cell line BT20 has been in culture, especially it is well known in the art that cell lines could have been in culture for years and years. Further, there is a widespread belief in the scientific community that cells in culture culture are not representative of the tumors from which they were derived, due to extensive chromosomal rearrangements, oncogene mutations, and multiple sites of allelic loss and gene amplification in tumor cell lines, including breast carcinoma cell lines, as taught by Drexler et al, Embleton et al, Hsu et al, Ozen et al, Freshney et al, Dermer et al.

Thus, in view of the above, it is unpredictable that the cell line BT20 has any of the properties of the cell lines studied by Wistuba et al, and retain many of the properties of their parental tumors, and one cannot determine whether that the putative overexpression of the claimed sequence in the breast cell line BT20 is not due to cell culture artifacts.

Moreover, it seems that the microarray used in the instant application for screening the overexpression of the claimed polynucleotide seems to be underrepresentative of all the mRNAs in the target cells, because the UNIGEM V microarray represents only 4610 annotated genes (specification, page 36, lines 20-21), which are far below the most recent estimates of the human genome projected approximately 30,000 genes, as recited by Appellant. Further, analysis of a microarray which is composed of cDNAs immobilized on glass slides (specification, page 36, lines 25-26) is similar to analysis of a substractive cDNA library in that a microarray or a

cDNA library has to be representative of mRNAs in a cell. A complete cDNA library is one that contains at least one cDNA clone representing each mRNA in a cell, and that there are about 34,000 different types of mRNAs in a mammalian cells and about 500,000 mRNA molecules per cell, as taught in a commonly used text book by Ausubel et al, eds, 1987 (Current protocols in molecular biology, John Wiley & Sons, New York, p. 5.8.1, under Production of a cDNA library). Ausubel et al further teach that if the number of molecules of the rarest mRNA in a cell is 8, the calculated number of clones that should be screened to achieve a 99% probability that a cDNA will exist in the library is 324,000. Similarly, in another commonly used text book by Sambrook et al, eds, 1989 (Molecular cloning, a Laboratory manuall, 2nd ed, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, p.8.3-8.7). Sambrook et al teach that a typical mammalian cell contains between 10,000 and 30,000 different mRNA sequences. Sambrook et al further teach that for low abundance mRNAs, i.e. 14 copies/cell, although the minimum clones required to obtain representation of mRNAs of this class is 37,000, but because of preferential cloning of certain sequences, a much larger number of recombinants must be obtained to increase the chances that any given clone will be represented in the library, i. e., about 170,000 clones (Sambrook et al, p.8.5 last paragraph, bridging p.8.7). Sambrook et al also teach that unfortunately, many mRNAs of interest are present at even lower level, i.e. 1 molecule/cell is not unusual. Thus based on the teaching in the art, it is clear that the microarray used in the claimed invention would not be representative of all mRNAs present in a cell. The fact that the claimed polynucleotide is not expressed in one set of microarray or is expressed in another

appears to be an artifact of the analytical system and cannot be extrapolated to a prediction of whether that molecule is expressed in the tissue "represented" by the microarray. It is not possible to determine from the information in the specification whether SEQ ID NO:2 could be useful in cancer research or as a marker for cancer cells without further research on the material itself.

Applicant argues that the Examiner has ignored that the claimed polynucleotides and the encoded polypeptides thereof have specific, substantial and credible utilities, in for example, toxicology testing in drug discovery, particulary drug discovery related to treatment of breast cancer.

Applicant recites that the Declaration by Dr. Tod Bedilion describes the use of the claimed polynucleotides in microarray of the type first developed at Standford University for gene expression monitoring, for evaluating the efficacy and toxicity of drugs, and thus useful in developing drugs and monitoring their activity.

Applicant characterizes the Bedilion declaration as describing some of the practical uses of the claimed invention in gene and protein expression monitoring applications, thus allegedly demonstrating the examiner's position to be without merit. In particular, Applicant states that the Bedilion declaration describes how the claimed expressed polynucleotide can be used in gene expression monitoring systems that were well-known at the time of the invention, and how those applications are useful in developing drugs and monitoring their activity. Applicant quotes from the Bedilion declaration, that states that microarrays containing SEQ ID NO: 1-encoding polynucleotides would be a more useful tool than microarrays lacking same in

connection with conducting gene expression monitoring studies on proposed or actual drugs for treating cell proliferative and developmental disorders for such purposes as evaluating their efficacy and toxicity.

This is not found to be persuasive. As an aside, it is noted that Dr. Bedilion is a consultant for Incyte Pharmaceuticals, Inc., the real party in interest in this appeal, and thus is a concerned party. Regarding the merit of the argument, any new polynucleotide can be used in a microarray, and thus this asserted utility is not specific. Also, the disclosure that the polypeptide encoded by the claimed polynucleotide is structurally related to mucin genes, and that the claimed polynucleotide is overexpressed in breast cell line BT20 in culture does not render the asserted utility specific, since the specification does not establish that the claimed polynucleotide is expressed in any diseased tissues in any way that is different from the way it is expressed in healthy forms of the same tissues. In other words, the specification does not disclose that the claimed polynucleotide is expressed in tissues having cell proliferative or developmental disorders at altered levels or in variant forms. Thus, it is not a target for drug development, toxicology studies, or disease diagnosis. Significant further research would have to be conducted to identify diseases states which correlate with altered levels or forms of the claimed polynucleotide. Therefore, this asserted utility is also not substantial.

Applicant discusses the Bedilion declaration's detailed explanations of how cDNA technology can be used to conduct gene expression monitoring evaluations. Applicant points to Dr. Bedilion's pages of text and numerous subparts explaining the importance

of this technology. Applicant points to Dr. Bedilion's explanation that those skilled in the art at the time of the invention without any doubt would have appreciated the criticality of toxicity testing.

The argument is not found to be persuasive. There is no doubt that cDNA microarray technology is an extremely valuable technique in gene expression monitoring, toxicology testing, and drug efficacy testing. However, the claims are not drawn to the technique. The claims are directed to polynucleotides which have not been disclosed as being associated with any particular disease or condition by its being expressed at an altered level or form in diseased tissue as compared to the corresponding healthy tissue. Any such polynucleotide could be added to a microarray. Thus, this asserted utility is not specific. Determining the relationship between the claimed polynucleotides and any specific disease or disorder would require significant further research. Therefore, this asserted utility is also not substantial.

Applicant urges that the Bedilion declaration establishes that persons skilled in the art, guided by the instant specification, at the time of the invention would have wanted their cDNA microarrays to comprise the claimed polynucleotide, because a microarray comprising the claimed polynucleotide would provide more useful results in the kind of gene expression monitoring studies that microarrays lacking the claimed polynucleotide.

This is not found to be persuasive. The specification has not linked the claimed polynucleotide with any specific disease state or disorder, as discussed above and in previous Office Actions. Adding the claimed polynucleotide to a microarray would not

make the microarray any more valuable than adding any other "orphan" polynucleotide. The asserted utility is not specific to the claimed polynucleotide.

Applicant argues that the examiner does not address the fact that, as described on page 14 of the specification, the claimed polynucleotide can be used as highly specific probes to measure both the existence and amount of complementary mRNA sequences known to be expression products of the claimed polynucleotides. Applicant concludes that the claimed invention is not, in that regard, some random sequence whose value as a probe is speculative or would require further research to determine.

This is not found to be persuasive. Any polynucleotide is a highly specific probe for itself or its complement, or any mRNA that can be transcribed from it. However, unless the significance of detecting the mRNA is known, because of some correlation between its expression and a condition or illness or function, then the use of a nucleic acid to probe for such expression constitutes at best, further research and not a substantial utility.

Applicants refer to Dr. Bedilion's discussion of the Brown et al. Patent (U.S. 5807522), attached to the declaration. Dr. Bedilion characterizes the patent as providing evidence that microarrays can be used in numerous genetic applications, including monitoring of gene expression in different tissue types, disease states, in response to drugs, and in response to potential toxins.

This is not found to be persuasive. The Brown patent claims methods of forming microarrays. Microarray methods have patentable utility as a research tool, just like a scale or a gas chromatograph. However, what the research tool measures does not

necessarily have patentable utility, such as the object being weighed by the scale, or the compound being analyzed by the gas chromatograph. Such is the situation at issue.

Applicant further asserts that use of proteins expressed by human as a tool for toxicology testing, drug discovery and diagnosis of disease is a well-established utility as confirmed by Rockett et al, Lashkari et al, and that the claimed polynucleotide could be used in array experiments to study the effect of toxicological compounds, as indicated in the email from Dr. C. Afshari to the undersigned. Applicant concludes that there is no expressed gene which is irrelevant to screening for toxicological effects, and all expressed genes have a utility for toxicological screening, and that the claimed polynucleotides could be used in this manner.

The argument is not found to be persuasive, because for a utility to be "well-established" it must be specific, substantial and credible. In this case, as indicated by Appellant in the response, all nucleic acids and expressed genes are in some combination useful in toxicology testing, or useful as a tool for research. However, the particulars of toxicology testing with the claimed polynucleotide of SEQ ID NO:2 are not disclosed in the instant specification. Neither the toxic substances nor the susceptible organ systems are identified from drug screening using microarrays. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to SEQ ID NO: 2. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet

been disclosed, the utility is not substantial because it is not currently available in practical form.

Moreover, use of the claimed polynucleotides in an array for toxicology screening or expression profiling is only useful in the sense that the information that is gained from the array or profile is dependent on the pattern derived from the array or profile, and says nothing with regard to each individual member of the array or profile. Again, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNAs. Even if the expression of Appellant's polynucleotides is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the claimed polynucleotides has no "well-established" use.

The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any expression information regarding the claimed polynucleotide and the encoded polypeptide could be put.

Applicant states that potential benefits to the public is enormous. Appellant cites 1) CV Therapeutics uses Incyte gene expression to identify the key gene associated with Tangiers disease, 2) reduction of time associated with target discovery and validation by Incyte customers, and 3) over 50% of the drug targets in the pipeline of Incyte customer are from Incyte database.

This is not persuasive because this assertion fails to address the utility of the individually claimed polynucleotides encoding SEQ ID NO:1, or the encoded

polypeptide. Further, in the absence of any disclosed relationship between the claimed polynucleotide and the encoded polypeptide and any disease or disorder and the lack of any correlation between the claimed polynucleotide and the encoded polypeptide with any known disease or disorder, any information obtained from a screening assay would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPO at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. 101.

The question at issue is whether or not the broad general assertion that the claimed polypeptides might be used for *some* diagnostic application, *some* drug discovery or *some* toxicology test (in the absence of a disclosure of *which* diagnostic application, *which* drug discovery or *which* toxicology test) would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPO 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to

show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates').

Applicant asserts that the use of the claimed invention as a tool for toxicology testing is a practical, real world use and is a "substantial" use. Applicant asserts that there is a vibrant market for databases containing all expressed genes. Applicant asserts that as used in toxicology testing, drug discovery and disease diagnosis the claimed invention has a beneficial use in research other than studying the claimed invention itself.

This is not persuasive because the evidence of record is inadequate to determine the disease(s), drug(s) or toxicological screen(s) for which the compounds would be useful. In *Brenner*, the Court approved a rejection for failure to disclose any utility for a compound where the compound was undergoing screening for possible tumor-inhibiting effects and an adjacent homologue of the compound had proven effective. *Brenner*, 148 USPO at 690. Here, there is no evidence that the claimed polynucleotide encoding SEQ ID NO:1 or the polypeptide encoded thereby has any utility.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Claims 1-6 remain rejected under 112, first paragraph, enablment due to lack of a specific, substantial utility or a well established utility for reasons already of record.

The same arguments and reasons for rejection as set forth under 101 rejection apply here as well.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 1-6 remain rejected under 112, first paragraph for lacking a clear written description of a polynucleotide encoding a naturally occurring amino acid sequence having at least 90% sequence identity to SEQ ID NO:1, or a naturally occurring polynucleotide having at least 90% sequence identity to SEQ ID NO:2, for reasons already of record .

Applicant asserts that given SEQ ID NO:1 and 2, and the described chemical, physical and structural features of SEQ ID NO:1, and coupled to what is conventional or well known, one of kill in the art would recognize naturally occurring variants of SEQ ID NO:1, having at least 90% sequence identity to SEQ ID NO:1

The argument is not found to be persuasive. Contrary to Applicant's assertion, the subject matter of the present claims is not defined in terms of the chemical structure of SEQ ID NOs:1 and 2.

The claims as written clearly read on allelic variant polynucleotides of the polynucleotide of SEQ ID NO:2, or allelic polynucleotides encoding variant polypeptides of the polypeptide of SEQ ID NO:1. No disclosure of the claimed allelic variant polynucleotides beyond the mere mention of variants and allelic sequences is made in the specification. The claims encompass allelic variant polynucleotides encoding polypeptide variants having any type of substitution by nature besides conservative substitution, or deletion by nature at any amino acid, throughout the length of the peptide, provided the changes are within 10% of the sequence identity. The specification does not disclose which amino acid subjected to conservative or non-conservative substitution, or deletion by nature, the type of substitution besides

conservative substitution by nature, nor the type of amino acids replacing the original amino acids. Thus the scope of the claims includes numerous structural polynucleotide variants. No common structural attributes that identify the claimed polynucleotide variants are disclosed. In addition, no common functional attributes that identify the claimed polynucleotide variants are disclosed, because the function of a polypeptide encoded by a polynucleotide could be abolished, even with substitution of only one amino acid of the polypeptide (Burgess et al), and because the function of SEQ ID NO:1 is not known (see the above Utility rejection). The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the claimed naturally occurring polynucleotide variants, SEQ ID NOs:1 and 2 alone are insufficient to describe said variants. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of polynucleotide variants and that Appellant was not in possession of the naturally occurring variant polynucleotides, and polynucleotides encoding naturally occurring polypeptide variants.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

Claims 1-6 remain rejected under 112, first paragraph for lacking enablement for a polynucleotide encoding a naturally-occurring amino acid sequence having at least 90% sequence identity to SEQ ID NO:1, or a naturally occurring polynucleotide having at least 90% sequence identity to SEQ ID NO:2, for reasons already of record.

Applicant asserts that Appellant has previously established utility for the polynucleotide of SEQ ID NO:2 and the polypeptide of SEQ ID NO:1 for reasons discussed previously in this brief. Applicant asserts that the use of the claimed variants in hybridization, amplification, and screening technology to identify and distinguish among SEQ ID NO:2 and related molecules in a sample is fully enabled by the specification.

This argument is not found to be persuasive. Applicant has not taught how to use the invention for the reasons previously set forth for utility. Thus since there is no practical, specific, and substantial uses for the sequence of SEQ ID NO:2, or the predicted encoded SEQ ID NO:1 and variants thereof in diagnosis of disease conditions, or in microarray for reasons set forth in utility rejection, other cited uses of the claimed variants of SEQ ID NO:2 such as hybridization probes, chromosome mapping, amplification, and screening technology to identify and distinguish among SEQ ID NO:2 and related molecules in a sample would not have any practical use either.

Further, no consensus sequences that identify the claimed polynucleotide variants are disclosed, *supra*, and thus one cannot identify and make the claimed variants.

Moreover, identification of the claimed variants, based solely on sequence homology would result in compounds with unknown function, since the unpredictability of utilizing predicted structural determinations to ascertain functional aspects of the protein is demonstrated by Bork and Scott et al, *supra* (see rejection under 101, utilty above), and thus one cannot predict that the claimed naturally occurring variants that

are screened by PCR, based solely to 95% identity with SEQ ID NO:or 2 would function as claimed . Bork teaches the pitfalls associated with comparative sequence analysis for predicting protein function and specifically states that conclusions from comparison analysis are often stretched with regard to protein products and specifically cites that most features predicted with an accuracy of greater than 70% are of structural nature and at best only indirectly imply a certain functionality. The teaching of Scott et al further confirms the teaching of Bork, wherein Scott et al teach an example of misidentification of the function of a protein based on homology alone, and conclude that it is important to confirm the function of a newly identified gene products even when the database reveal significant homology to proteins of known function.

Thus, one of skill in the art would not know how to use the claimed variants based solely on screening sequences having sequence homology to SEQ ID NO:2, nor how make a polynucleotide encoding a naturally-occurring amino acid sequence having at least 90% sequence identity to SEQ ID NO:1, or a naturally occurring polynucleotide having at least 90% sequence identity to SEQ ID NO:2, so that they would function as claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone

number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

January 09, 2004

SUSAN UNGAR, PH.D
PRIMARY EXAMINER